REMARKS

Applicant wishes to thank the Examiner for the consideration given this case to date and for the courtesies extended by Examiners Blanchard and Helms during the Examiner's interview conducted on October 15, 2004.

Applicant respectfully submits that the application, as amended, is now in condition for allowance. Originally, claims 1-68 were filed with this application. Claims 1-13 are presently amended and acknowledged as being withdrawn by the Office being generic claims, subject to further consideration by the Examiner pending examination of the restricted claims and species. Claims 14-68 are cancelled as being drawn to a nonelected invention. Applicant reserves the right to prosecute claims 14-68 and like claims in future applications. Claims 69-115 are new and presented pursuant to the Examiner's restriction requirement.

THE EXAMINER'S ACTION

In the Office Action dated May 20, 2004, the Office:

-made the restriction requirement final;

-objected to the specification, as described in the paragraphs below;

-rejected claims 6 and 13 under 35 U.S.C. 112, second paragraph, as being indefinite;

-rejected claims 1-13 under 35 U.S.C. 112, first paragraph, for lack of enablement;

-rejected claims 1, 2 and 7-10 under 35 U.S.C. 102(b) based on Noguchi et al. (Proc. Natl. Acad. Sci. USA; 92:2219-2223, 1995; "Noguchi") and Trinchieri (Immunol. Today 14:335-338, 1993; "Trinchieri"); and

-rejected claims 1-5 and 7-12 under 35 U.S.C. 103(a) based on Apostolopoulos et al. (Vaccine 14:930-938, 1996; "Apostolopoulos") in view of Tachibana et al. (Tokai J. of Exptl. Clin. Med. 8:455-463, 1983; "Tachibana"), Trinchieri, Parkhouse et al. (Curr. Topics Microbiol. & Immunol. 182:331-335, 1992; "Parkhouse") and Wang (U.S. Pat. No. 5,939,380; "Wang").

SPECIFICATION

Applicant has amended the application, as requested by the Examiner, to update the priority information in the first line of the specification with a benefit claim to Application serial

numbers 60/103,350 and 60/117,526.

Applicant has amended the application to delete the segmented line on page 21, line 20, as requested by the Examiner.

The objection to the Brief Description of Drawings as set forth on page 3 of the Office Action dated May 20, 2004 was discussed in the interview with the Examiner. For completeness of the written record, the meaning of the lines numbered 1 through 4 in Figure 4 is stated beginning on page 39, line 22 of the application and continuing through page 40, line 3. Likewise, the meaning of the line numbered 5 in Figure 4 is stated beginning on page 49, line 26 of the application through page 50, line 5. Applicant respectfully requests that the objection to the Brief Description of Drawings therefore be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-13 have been acknowledged as being withdrawn, rendering this rejection moot.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner rejected claims 1-13 as not enabling a vaccine composition for preventing a solid nonlymphoid tumor.... As stated on page 5 of the Office Action, the Examiner noted that an immunotherapeutic composition for treating a solid nonlymphoid tumor was enabled.

As an initial matter, Applicant notes that the claims as filed called for a vaccine composition "for suppressing" and "for inducing." Applicant asserts that the entire specification enabled such a vaccine.

Second, claims 1-13 have been acknowledged as being withdrawn, while new claims 69-115 are believed to comply with section 112, first paragraph. For example, the claims call for compositions broader than vaccines such as immunotherapeutic compositions generally. Moreover, the claims now call for compositions that suppress, treat, inhibit, overcome, etc. For either or both reasons, Applicant respectfully asserts that the rejections are overcome.

REJECTIONS UNDER 35 U.S.C. § 102(b) AND 35 U.S.C. § 103(a)

Claims 1, 2, and 7-10 were rejected under 102(b) in light of Noguchi and Trinchieri. Claims 1-5, and 7-12 were rejected under 103(a) in light of Apostolopoulos in view of Tachibana, Trinchieri, Parkhouse and Wang. As discussed, Applicant's claims are distinguished from the cited art based on the discussion below.

Beginning on page 21, line 23, and extending to page 22, line 4, the specification recites:

> The present invention relates to: (a) the discovery of a humoral immune response, "a pro-tumor immune response", which may be present in individuals bearing solid nonlymphoid tumors; and (b) that in an individual having a pro-tumor immune response, the pro-tumor immune response has a propensity (e.g., as mediated through activated B cells, immune complexes, and activated immune effector cells) to: selectively drive the immune response, in polarizing the immune response, to comprise a TH2 response; preserve an immune response polarized to a TH2 response; and to suppress a cell mediated immune response comprising a TH1 response (as exemplified by a TH2/TH1 imbalance).

As defined on page 18, lines 16-28 of the specification, a pro-tumor response is a humoral immune response induced by carbohydrate epitopes of shed tumor antigen. Shed tumor antigen is defined, beginning on page 17, line 14, and extending to page 18, line 15 of the specification. The specification also recites that TH2 cells secrete cytokines that include IL-4, IL-6, and IL-10, and that a TH2 response is characterized by these cytokines (see, e.g. page 1, lines 18-19 and page 2, lines 19-27 of the specification). As recited in the specification, in the TH2/TH1 imbalance that is found in a pro-tumor immune response, the TH2 cytokines inhibit TH1 cell development (page 22, lines 15-20 of the specification) and suppress a TH1 pattern of cytokine production (page 23, lines 10-15 of the specification). Figures 1-3 of the application show that shed tumor antigen and antibody to anti-shed tumor antigen promote and sustain the TH2 response and the TH2/TH1 imbalance, which includes significant production of IL-4 (see also pages 32 and 33 of the specification).

As discussed in the Examiner Interview, the claims are distinguished from the prior art references cited by the Office in the Action dated May 20, 2004. In particular, an element in the claims is that the claimed composition is effective against the TH2/TH1 imbalance in a pro-tumor immune response. This element is missing, for example, in the Apostolopoulos reference.

Apostolopoulos teaches induction of a humoral immune response to a mucin peptide (amino acid epitopes of mucin backbone) fused to GST, and fail to teach or suggest a humoral immune response, a pro-tumor immune response, induced by shed tumor antigen; and more particularly induced against a terminal (exposed) carbohydrate antigen of the shed tumor antigen (as even noted by Apostolopoulos on page 930, column 1, lines 1-5). In addition to describing a totally different antigen (protein rather than carbohydrate), Apostolopoulos describes a totally different humoral immune response; i.e. no TH2/TH1 imbalance is described with peptide antigens, and Apostolopoulos further discloses that there is not a lack of a T-cell response to such peptide epitopes (Apostolopoulos on page 936, column 1, lines 13-18).

Additionally, the claims are distinguished from the references cited by the Examiner, for example, in that both the Trinchieri reference and the specification teach away from combining the cited references. In particular, as discussed with the Examiners, IL-12 should not be interpreted as an effector of B cell depletion in the context of a TH2/TH1 imbalance. Trincheri shows that IL-4 is a major cytokine produced during a TH2 response, and the "effect of IL-4 is, however, dominant over that of IL-12 (Trincheri, page 337 column 1, lines 35-37). Further, "once a TH1 or TH2 type of response is determined early during the immune response, it remains stable, unless major changes take place in the balance of cytokine production during the response" (Trincheri, page 337 column 2, lines 42-48).

That IL-12 should not be interpreted as an effector of B cell depletion is also supported in the specification as filed (see, e.g., page 40, lines 4-13; and Figure 4). Treatment of mice with IL-12 (in combination with B cell depletion) increased the rate of tumor recurrence compared to the other treated groups shown in Figure 4. In specifically illustrating this point, treatment with an anti-B cell agent and IL-12 (Figure 4, line 3) was significantly less effective in preventing recurrence of tumors than treatment with the anti-B cell agent alone (Figure 4, line 2), suggesting that the IL-12 reduced - rather than promoted - B cell depletion.

Based on the above discussion and summary of arguments made during the Examiner's interview, Applicant's claims are distinguished from and patentable over, the cited art. Applicant respectfully asserts that the rejections are overcome and that the claims are allowable.

CONCLUSION

For the foregoing reasons, Applicant respectfully asserts that the case is now in a condition for allowance. The Commissioner is hereby authorized to charge any additional fees, or credit any overpayment to Deposit Account No. **02-2051**, referencing Attorney Docket No. **26983-98 (B-63)**.

Respectfully submitted,

Dated: October 20, 2004

W. Scott Harders
Reg. No. 42,629

BENESCH, FRIEDLANDER COPLAN & ARONOFF LLP
2300 BP Tower
200 Public Square
Cleveland, OH 44114-2378
(216) 363-4443